<Bioinformatics Center> Bioinformatics Training Unit

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Prof
TOH, Hiroyuki
(D Sc)

Assoc Prof
KUMA, Keiichi
(D Sc)

Assist Prof
DAIYASU Hiromi
(D Sc)

Assist Prof
ICHIHARA Hisako

PD
KATOH, Kazutaka
(D Sc)

PD
HOSHIYAMA, Daisuke
(D Sc)

PD
YOKOI, Toshiro
(D Agr)

Students

YAMAGUCHI, Takeshi (D5)
NEMOTO, Wataru (D2)
SATO, Tetsuya (D1)

Visitor

PILS, Birgit
Department of Bioinformatics, Wurzburg University, Germany,
6 July - 22 August 2004

Scope of Research

Evolutionary studies based on molecular biology is called “molecular evolutionary biology”, which is one of the origins of the current bioinformatics. Living organisms have acquired wide variety of functions during the course of the evolution by changing the information encoded by the genomes. Inversely, reconstruction of the evolutionary history related to the functions would bring us a great insight into the acquired functions and the life. Furthermore, such evolutionary information is useful for practical fields such as drug design and proteins engineering. We develop new methodologies with evolutionary information, to extract biological knowledge from various molecular biological data including sequence and structure data of individual genes and proteins, genome data, and expression profile data. We also analyze the data of molecular biology from the evolutionary viewpoint, to obtain novel biological knowledge.

Research Activities (Year 2004)

Presentations

Prediction of Interfaces for the class A GPCR oligomerization, Nemoto W, Toh H, 1st Pacific-Rim International Conference on Protein Science, 15 April.

Evolutionary analysis of membrane-associated proteins, Toh H, Ichihara H, Daiyasu H, 1st Pacific-Rim International Conference on Protein Science, 16 April.

Investigation of the cause of rate reduction observed in higher vertebrates, Hoshiyama D, Kuma K, Toh H, Miyata T (JT Biohistory Research Hall, Waseda University), Society of Evolutionary Studies, Japan 6th Annual Meeting, 6 August.

MAFFT: a multiple sequence alignment program, Katoh K, Misawa K (Kazusa DNA Research Institute), Kuma K, Toh H, Miyata T (JT Biohistory Research Hall, Waseda University), 76th Annual Meeting of the Genetics Society of Japan, 28 September.

Molecular evolution of polar lipid biosynthesis in Archaea, Toh H, Yokoi T, Daiyasu H, 27th The Molecular Biology Society of Japan, 8 December.

Computational Analysis of Substrate Specificity of Disaccharide-Specific Glycosidase, Daiyasu H, Mizutani M, Sakata K, Toh H, 27th The Molecular Biology Society of Japan, 9 December.

Optimized MAFFT: improvement in accuracy of multiple sequence alignment, Katoh K, Kuma K, Toh H, Miyata T (JT Biohistory Research Hall, Waseda University), 27th Annual Meeting of the Molecular Biology Society of Japan, 9 December.

Database for GPCRs Interaction Partners -GRIP-, Nemoto W, Toh H, 27th The Molecular Biology Society of Japan, 9 December.

Estimation of divergence time between Chlorella and land plants, and molecular evolution of Chlorella TPI

Basal Jawed Vertebrate Phylogeny Inferred from Multiple Nuclear DNA-coded Genes

We have cloned and sequenced seven nuclear DNA-coded genes from 13 vertebrate species. These sequences, together with sequences available from databases including 13 jawed vertebrates from eight major groups (cartilaginous fishes, bichir, chondrosteans, gar, bowfin, teleost fishes, lungfishes and tetrapods) and an outgroup (a cyclostome and a lancelet), have been subjected to phylogenetic analyses based on the maximum likelihood method. Cartilaginous fishes have been inferred to be basal to other jawed vertebrates, which is consistent with the generally accepted view. The minimum log-likelihood difference between the maximum likelihood tree and trees not supporting the basal position of cartilaginous fishes is 18.3 ± 13.1. Our tree has also shown that living holosteans, comprising bowfin and gar, form a monophyletic group which is the sister group to teleost fishes. This is consistent with a formerly prevalent view of vertebrate classification, although inconsistent with both of the current morphology-based and mitochondrial sequence-based trees. Furthermore, the bichir has been shown to be the basal ray-finned fish. Tetrapods and lungfish have formed a monophyletic cluster in the tree inferred from the concatenated alignment, being consistent with the currently prevalent view. It also remains possible that tetrapods are more closely related to ray-finned fishes than to lungfishes.

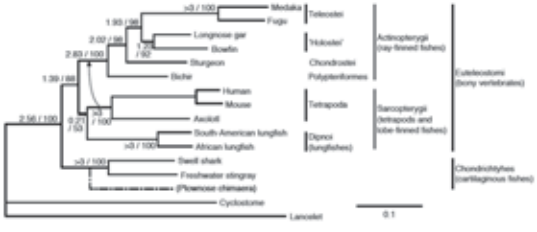

Figure 1. The maximum likelihood tree inferred from the concatenated amino acid sequences (2,942 residues) of seven proteins.

Identification of Cryptochrome DASH from Vertebrates

A new type of cryptochrome, CRY-DASH, has been recently identified. The CRY-DASH proteins constitute the fifth subfamily of the photolyase/cryptochrome family. CRY-DASHs have been identified from *Synechocystis* sp. PCC 6803, *Vibrio cholerae,* and *Arabidopsis thaliana.* The *Synechocystis* CRY-DASH was the first cryptochrome identified from bacteria, and its biochemical features and tertiary structure have been extensively investigated. To determine how broadly the subfamily is distributed within living organisms, we searched for new CRY-DASH candidates within several databases. We found five sequences as new CRY-DASH candidates, which are derived from four marine bacteria and *Neurospora crassa.* We also found many CRY-DASH candidates from the EST databases, which included sequences from fish and amphibians. We cloned and sequenced the cDNAs of the zebrafish and *Xenopus laevis* candidates, based on the EST sequences. The proteins encoded by the two genes were purified and characterized. Both proteins contained folate and flavin cofactors, and have a weak DNA photolyase activity. A phylogenetic analysis revealed that the seven candidates actually belong to the new type of cryptochrome sub family. This is the first report of the CRY-DASH members from vertebrates and fungi.

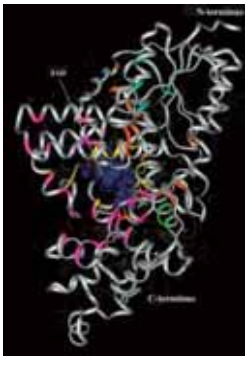

Figure 2. Mapping of the residues corresponding to the invariant sites within the CRY-DASH subfamily on the *Synechocystis* CRY-DASH structure.

genes, Kuma K, Yokoi T (Hitachi, Ltd.), Harada Y (Hitachi, Ltd.), Mizoguchi T (Sun Chlorella Corp.), 27th The Molecular Biology Society of Japan, 10 December.

Prediction of Protein-Protein Interactions Based on Real-Valued Phylogenetic Profiles Using Partial Correlation Coefficient, Sato T, Yamanishi Y, Kanehisa M, Toh H, 15th International Conference on Genome Informatics, 13-14 December.

Grants

Toh H, Development of the tools for protein structure comparison, BIRD, 1 April 2004 - 31 March 2005.

Toh H, Domain Prediction in Structural Genomics for Signal Transduction (Inagaki group), Protein 3000, 1 April 2004 - 31 March 2005.

Toh H, Development of the Computational method to analyze soft protein-protein interactions, Grant-in-Aid for Scientific Research, 1 April 2004 - 31 March 2005.

Award

Toh H, The Okawa Publications prize, Bioinformatics for the Analysis of Protein Function, The Okawa Foundation, 25 November.